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MYOCARDIAL ISCHEMIA AND INFARCTION

THE β1 BLOCKER/β3 AGONIST NEBIVOLOL PROTECTS AGAINST ACUTE MYOCARDIAL INFARCTION IN MICE

ACC Poster Contributions
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Background: Nebivolol (NEB) is a third generation (β1AR) antagonist and β3-adrenoceptor (β3AR) agonist currently used to treat hypertension. Studies indicates that β3-AR activation promotes eNOS activity and nitric oxide (NO) generation. We hypothesized that acute NEB therapy attenuates the severity of myocardial ischemia-reperfusion (MI-R) injury via β3-AR stimulation, eNOS activation, and increased NO bioavailability.

Methods: Mice were subjected to 45 min of MI in vivo followed by R for 24 hr. NEB (500 ng/kg) or vehicle (VEH) was administered via intracardiac injection at the time of R. At 24 hr of R myocardial area-at-risk (AAR) per left ventricle (LV) and infarct size per area-at-risk (INF/AAR) were evaluated using Evan's Blue and TTC. Serum troponin-I levels were also measured. In separate studies, cardiac tissue and plasma samples were collected from mice treated with NEB or VEH following a single injection to evaluate eNOS phosphorylation (eNOS-P) status as well as plasma nitrite and nitrosothiol levels.

Results: NEB significantly reduced INF by 39% ($p < 0.001$ vs. VEH) and serum troponin-I levels were reduced from 41±4 to 25±4 ng/mL ($p < 0.05$ vs. VEH). Furthermore, we observed an increase in cardiac eNOS-P of Ser-1177 ($p < 0.001$ vs. VEH) and a 2-fold increase ($p < 0.05$ vs. VEH) in plasma nitrite and nitrosothiol levels following NEB treatment.

Conclusion: Our results indicate that the protective effects of NEB during acute MI-R are mediated by eNOS activation and increased NO and nitrite bioavailability.